REMARKS

The Office Communication, mailed December 17, 2002, has been received and reviewed. Claims 1-22 are pending and stand rejected. Claims 2-3, 5-6, 9-12, 15, 17 and 20 have been canceled without prejudice or disclaimer. Claims 1, 4, 7-8, 13-14, 16, 18-19 and 21 are currently pending. Reconsideration and withdrawal of the rejections are respectfully requested.

I. Correction of the Drawings:

The drawings are objected to for the reasons set forth in PTO Form 948. Figures 2-4 and 6-11 are objected to for non-acceptable top and bottom margins. Figures 1-5 are objected to for having poor quality lines. Figure 1 is objected to for inclusion of a border.

The applicants are herewith submitting corrected drawings in a separate letter to the Chief Draftsperson.

II. Objection to the Oath or Declaration:

The Declaration is objected to as allegedly having non-initialed and/or non-dated alterations to the address of Abraham Bout. The applicants herewith submit a new declaration.

III. Objection to the Abstract:

The Abstract is objected to for containing the legal term "means." The applicants have amended the Abstract to remove this term. Reconsideration and withdrawal of the objection is respectfully requested in light of the amendment to the Abstract.

IV. Objection to Claim 2:

Claim 2 is objected to for the absence of "a" between the words "by" and "viral." The applicants have canceled claim 2, mooting the rejection.

V. Rejection of Claims 1-22 under 35 U.S.C. § 112, first paragraph:

Claims 1-18 and 20-22 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking a sufficient written description commensurate with the scope of the claims. The broadest

claims were thought to include any type of gene delivery vehicle, and the specification was thought to only disclose adenovirus vectors. The Office further alleges that the more narrowly drawn claims do not include a limitation that the capsid is necessarily an adenoviral capsid. It was further asserted that the only fibers shown to provide tissue tropism for dendritic cells were obtained from Ad11, Ad16, Ad35, Ad51 or Ad40L. The Office then asserts that because the prior art teaches that predicting the tertiary structure of a protein, given its primary sequence, is not well understood and not predictable, citing Berendsen, the skilled artisan could not envision additional adenoviral fibers providing the recited tissue tropism based on the teachings of the instant specification.

To expedite prosecution of the application the claims have been amended to overcome the rejection. However, the applicants respectfully traverse this rejection for at least the following reasons. The gene delivery vehicle used in the primary examples is an adenovirus, however, other gene delivery vehicles may be modified as per the teachings of the instant specification to provide tropism to dendritic cells. For example, capsid proteins of other viruses can be modified so as to include a chimeric protein having a fragment of an adenovirus fiber protein, wherein tropism to dendritic cells is provided. Furthermore, the applicants have disclosed five (5) fiber protein fragments that provide the claimed tropism. The applicants need not disclose each and every fiber fragment capable of producing this tropism, so long as the specification discloses to a person of ordinary skill in the art how to make and use the invention. The applicants submit that the instant specification discloses a sufficiently large number of species to enable the genus of fiber proteins which produce tropism to dendritic cells. Specifically, the Office has specifically acknowledged that "[t]he prior art appears to be silent with regard to chimeric viral capsids comprising protein fragments that are intended to direct the recombinant capsid to dendritic cells" (Page 3 of paper 5). The applicants have described novel chimeric capsids, having a protein fragment that directs the recombinant capsid to dendritic cells.

While the applicants respectfully traverse the grounds for rejection, the claims have been amended to overcome the rejection. Specifically, the claims, as amended, are directed to an adenoviral vector or capsid of subgroup C and to those adenoviral fibers obtained from Ad 11, Ad 16, Ad 35, Ad 51 or Ad 40L. Reconsideration and withdrawal of the rejection are

respectfully requested in light of the amendments.

Claims 1-22 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly being indefinite. Claim 1 is alleged to be vague and indefinite in that the metes and bounds of the phrase "having been provided with" is not clear. Claims 2, 5-6, 10-12 and 20 are alleged to be vague in that the metes and bounds of the phrase "derived from" is not clear, but that use of "obtained" would imply a more direct process. Claims 2, 5-6, 10-12 and 20 have been canceled without prejudice or disclaimer, thus, the rejection is moot as to them.

The applicants assert that "having been provided with" is clearly defined within the claim. Claim 1 recites "A gene delivery vehicle having been provided with at least a tissue tropism for dendritic cells wherein said tissue tropism for dendritic cells is provided by a viral capsid protein." Thus, the claim is directed to a gene delivery vehicle "having been provided with" a tissue tropism for dendritic cells, which is provided by a viral capsid protein.

However, the applicants have amended the claim to more particularly point out that the presently claimed source of tropism is the fiber protein. Reconsideration and withdrawal of the rejection is respectfully requested.

VI. Rejection of Claims 1-22 under 35 U.S.C. § 102(e):

Claims 1-22 stand rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Crystal *et al.* (U.S. Patent 6,127,525). The applicants traverse the rejection.

As acknowledged by the Office, Crystal *et al.* does not disclose tissue tropism for dendritic cells, wherein the tissue tropism for dendritic cells is provided by a viral fiber protein selected from the group consisting of adenovirus 11, Adenovirus 16, Adenovirus 35, Adenovirus 51 and Adenovirus 40L or a fragment thereof. Crystal *et al.* discloses chimeric capsid proteins to reduce or eliminate recognition by neutralizing antibodies. In Example 3, col. 24, line 55 to col. 25, line 27, Crystal *et al.* state that "switching the fiber from that of adenoviral serotype 5 group C vector to that of an adenoviral serotype 7 group B vector by itself is insufficient to allow the vector to escape neutralizing antibodies generated against an adenoviral vector comprising Ad5 fiber," col. 25, lines 15-19. Thus, Crystal *et al.* states that switching the fiber protein does not accomplish the purpose of ~~the invention~~ that patent (escape from the neutralizing antibodies). As a result of

this failure, Crystal *et al.* teaches away from the use of fiber proteins and, at most, amounts to an invitation to experiment for the purpose of no gain. *In re O'Farrell*, 853 F.2d 894, 901 (Fed. Cir. 1988).

Furthermore, Crystal *et al.* does not disclose tropism, and does not disclose or even mention dendritic cells. Therefore, Crystal *et al.* does not teach tropism for dendritic cells as recited in the pending claims. Moreover, Crystal *et al.* does not teach the use of a fiber protein (particularly, not Ad 11, Ad 16, Ad 35, Ad 51 or Ad 40L) for the purpose of achieving tropism and would not motivate a person of skill in the art to address the issue tropism.

The applicants respectfully disagree that Crystal *et al.* teaches capsids comprising the entire fibers obtained from Ad11, Ad16 or Ad35, at most, Crystal *et al.* suggests using Ad7 fiber proteins to escape neutralizing antibodies, but further teaches that such fiber proteins do not work in that regard. Thus, at most Crystal *et al.* only discloses a fiber protein from Ad7 for the purpose of avoiding neutralizing antibodies (a function which it failed to perform). Crystal *et al.* contains no disclosure of tropism. Crystal *et al.* can only be cited for the impermissible premise that it would have been obvious to try using the claimed fiber proteins to achieve a non-disclosed tropism. *Id.*

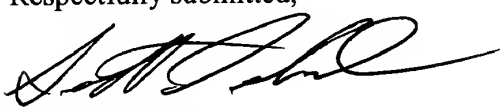
"Inherency ... may not be established by probabilities or possibilities." *Continental Can Company USA, Inc. v. Continental Pet Technologies, Inc.*, 948 F.2d 1264, 1269 (Fed. Cir. 1991). The possibility that the fiber protein of Ad7 may or may not function to target the virus to dendritic cells is a mere possibility. Furthermore, the Office has acknowledged that "[t]he prior art appears to be silent with regard to chimeric viral capsids comprising protein fragments that are intended to direct the recombinant capsid to dendritic cells." Therefore, Crystal *et al.* does not anticipate the claims.

Reconsideration and withdrawal of the rejection is respectfully requested.

CONCLUSION

In light of the amendments, the application is submitted to be in condition for allowance. If questions should remain after consideration of the amendments and remarks, the Office is kindly invited to contact the applicant's representative at the number provided herein.

Respectfully submitted,



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IN THE ABSTRACT:

Please replace the abstract on page 27 with the following clean copy:

Adenoviral vectors can be used in vaccines to cause antigen-presenting cells to display desired antigens. Disclosed is a vector and associated [means and] methods which transduce antigen-presenting cells better than currently available vectors, enabling the vector to be delivered in lower doses, and thus [improving] improves the efficiency of adenoviral vaccine technology.

IN THE CLAIMS:

1. (Amended) [A gene delivery vehicle] A recombinant chimeric adenoviral vector comprising an adenoviral vector having [been provided with at least] a tissue tropism for dendritic cells wherein said tissue tropism for dendritic cells is provided by a first adenovirus [viral] capsid [protein], wherein said first adenovirus capsid comprises a capsid fiber protein selected from the group consisting of adenovirus 11, Adenovirus 16, Adenovirus 35, Adenovirus 51 and Adenovirus 40L and a second adenoviral capsid obtained from adenovirus subgroup C.

4. (Amended) The [gene delivery vehicle] recombinant chimeric adenoviral vector of claim [3] 1 wherein said capsid fiber protein is Adenovirus 35. [at least one of said at least two different viruses is an adenovirus of subgroup B.]

7. (Amended) The [gene delivery vehicle] recombinant chimeric adenoviral vector of claim [4] 1, wherein said [subgroup B adenovirus is adenovirus] capsid fiber protein is Adenovirus 16.

8. (Amended) The [gene delivery vehicle] recombinant chimeric adenoviral vector of claim [5] 1, wherein said [subgroup B adenovirus is adenovirus] capsid fiber protein is Adenovirus 11.

13. (Amended) [The gene delivery vehicle of claim 1] A recombinant chimeric

adenoviral vector, comprising adenoviral nucleic acid, said adenoviral nucleic acid [comprising] encoding an adenovirus subgroup C viral capsid and at least one sequence encoding [a] an adenovirus fiber protein having at least a tissue tropism determining fragment of a [subgroup B adenovirus] fiber protein selected from the group consisting of adenovirus 11, Adenovirus 16, Adenovirus 35, Adenovirus 51 and Adenovirus 40L.

14. (Amended) The [gene delivery vehicle] recombinant chimeric adenoviral vector of claim 13, wherein said adenovirus nucleic acid is modified such that replication [the capacity] of said adenoviral nucleic acid [to replicate] in a target cell [has been] is reduced or disabled.

16. (Amended) The [gene delivery vehicle] recombinant chimeric adenoviral vector of claim 14, wherein said adenoviral nucleic acid is modified such that [the capacity of a host immune system to mount] an immune response against adenovirus proteins encoded by said adenovirus nucleic acid [has been] is reduced or disabled in a host system and said fiber protein is adenonvirus 35.

18. (Amended) The [gene delivery vehicle] recombinant adenoviral vector of claim [1] 14, further comprising at least one non-adenoviral nucleic acid.

19. (Amended) [An adenovirus capsid] A recombinant chimeric adenoviral capsid having a tissue tropism for dendritic cells wherein said adenovirus capsid comprises:

proteins from at least two different adenoviruses, and

a tissue tropism determining fragment of a fiber protein [derived] obtained from a subgroup B adenovirus selected from the group consisting of adenovirus 11, Adenovirus 16, Adenovirus 35, Adenovirus 51 and Adenovirus 40L.

21. (Amended) The [composition] recombinant chimeric adenoviral capsid of claim [20] 19 wherein [the] said fiber protein is Adenovirus 35. [adenovirus of subgroup B is selected from the group of adenoviruses consisting of Ad16, Ad35, Ad11, and Ad51.]